REVIEW

The longitudinal association between loneliness and depressive symptoms in the elderly: a systematic review

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ABSTRACT

Objective: Loneliness and the onset of depression in old age are growing problems related to the greater life expectancy nowadays. This review investigated the longitudinal association between loneliness and depressive symptoms in the elderly.

Design: A comprehensive search was conducted using three databases (Scopus, PsycInfo, and PubMed) combing for empirical studies published up until July 2020. A total of 4.549 abstracts and 221 full-text articles were assessed. Three authors independently reviewed titles and abstracts; disagreements were resolved by consensus.

Results: Ten studies were included in the final review. We identified two categories of studies based on the outcome considered in each article: 1) the longitudinal effect of loneliness on depressive symptoms and 2) the clinical course of depression and its association with loneliness. All the articles reported a significant and positive association between loneliness and depressive symptoms in their longitudinal design research, ranging from an odds ratio of 0.41 to 17.76. The heterogeneity regarding the effect size in the analyses can be explained by the multifactorial design implemented by most of the studies included.

Conclusions: Future research should investigate the moderators' role and how it may influence the longitudinal association between loneliness and depression over the years.

Key words: loneliness, depression, depressive symptoms, elderly, older, longitudinal

Introduction

The progressive aging of the global population, triggered by low fertility rates and longer life expectancy, is a global issue that requires research and policies to address the growing needs of the elderly.

Old-age loneliness has been of global concern for decades, but with the outbreak of COVID-19, and the consecutive pandemic measures applied the world over, such as lockdown and social distancing, it has shifted to become a primary concern to care-providing organizations and policymakers (Patel and Clark-Ginsberg, 2020). Stay-at-home orders may have affected social connectedness of the elderly and increased their loneliness, especially of those already living alone (Armitage and Nellums,

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2020). Concerns about the psychological well-being of elders who live alone and the devastating consequences of loneliness are receiving growing attention worldwide.

Loneliness becomes highly prevalent with age. Surveys in Europe and the USA estimated that the prevalence of loneliness ranges from 5% to 43% in the elderly (Djernes, 2006; Dykstra, 2009; Pinquart and Sörensen, 2000), making it an important issue. The causes may range from personal to societal factors. Since various critical events (e.g. loss of a spouse, admission to a nursing home, and loss of functional abilities) tend to occur later in life, loneliness is frequent in old age and has been shown to be an increasing challenge (Tesch-Roemer & Huxhold, 2019). For the elderly, loneliness is often associated with mental health problems (Luanaigh and Lawlor, 2008), cognitive decline (Martin et al., 1997; Shankar et al., 2013), poor self-rated health (Nummela et al., 2011), and increased mortality (Holt-Lunstad et al., 2015; Tilvis et al., 2011). Being

alone or living alone does not always imply the negative experience of loneliness. Although it may increase the risk of loneliness, not all elderly people who live alone feel lonely and vice versa. Being alone and loneliness are two well-distinguished concepts. Living alone becomes detrimental when it leads to loneliness. De Jong-Gierveld (1998) defined loneliness as "a situation in which the number of existing relationships is smaller than is considered desirable, as well as situations where the intimacy one wishes for has not been realized." A distinction must be made with social isolation, which refers to the more objective absence of social contacts (Routasalo *et al.*, 2006). It is important to note that there is no direct association between network size and loneliness. People with a small network may be socially isolated without experiencing feelings of loneliness (Townsend and Tunstall, 1973; Wenger *et al.*, 1996). Weiss (1973) distinguished two subtypes of loneliness: emotional and social. The former is related to the absence of one or more intimate figures, whereas the latter refers to the absence of a broader social network. Emotional loneliness refers to the absence of intimate relationships, whereas social loneliness has been defined as the absence of engaging social networks (De Jong-Gierveld and Kamphuis, 1985). The loss of a relation can be a significant trigger for emotional loneliness (Tiilikainen and Seppanen, 2017). Emotional loneliness may reveal itself to be particularly relevant when studying the elderly, as they are more likely to suffer bereavement. Older adults frequently report loneliness, which in turn has been proven to have a profoundly negative effect on depression (Cacioppe *et al.*, 2006). In a systematic review, the authors found that loneliness is detrimental not only to health, but it is also an independent risk factor for depression (O'luanaigh *et al.*, 2012).

Late-life depression is a complex and heterogeneous disorder that has been associated with a chronic course (Haigh *et al.*, 2018), a higher risk of subsequent development of cognitive impairment or dementia (Singh-Manoux *et al.*, 2017), and premature death (Blazer, 2003). Depression is one of the most common causes of disability, reducing life satisfaction in older people (Skoog, 2011). Old age seems to be significantly associated with a worse major depressive disorder. Studies estimate that from 3 to 16% of people may experience a depressive disorder in late life (Whiteford, 2013) and up to 10% may experience an unremitting and chronic course of depressive symptoms (de la Torre-Luque *et al.*, 2019). Prevalence of recurrent depression, characterized by a relapse in depression symptoms after a euthymic period, has been estimated to be between 25% and 40% (Richards, 2011). These results underscore the need to identify which factors in

the elderly have an impact on the recurrence of depressive symptoms. A systematic review found that the older population showed remission rates and response to treatment similar to those of middle-aged people, but relapse rates seemed higher in older age (Mitchell and Subramaniam, 2005). Another study reported how nearly half of depressed elders maintained their diagnosis even after 2 years, and that 61% had a chronic course of depressive symptoms (Comijs *et al.*, 2015). The recurrence, relapse, and chronicity of late-life depression are well-known problems in daily practice. A longitudinal study found that the average symptom severity of depressed elders remained above the 85th percentile of the population average for 6 years. Symptoms were short-lived in only 14% of patients. Twenty-three percent reported remissions, 44% an unfavorable, yet fluctuating course, and 32% maintained severe, chronic symptoms (Beekman *et al.*, 2002). Poor recovery from the depressive disorder has been shown to be related to low perceived social support (Leskelä *et al.*, 2006; Nasser and Overholser, 2005). Another cross-sectional study (Houtjes *et al.*, 2010) demonstrated that depression severity is associated with several unmet social needs of older patients.

Although major depressive episodes are less common in older age (1–4%), what is referred to as subclinical depression is a particularly relevant phenomenon (8–16%) (Alexopoulos, 2005; Blazer, 2003). Subsyndromal symptomatic depression or subthreshold depression (SSD) is defined as the presence of depressive symptomatology that does not meet the diagnostic criteria for a major depressive disorder (Meeks et al., 2011). Though SSD is not recognized as a formal disorder by the Diagnostic and Statistical Manual of Mental Disorders, it has been associated with multiple comorbidities including psychiatric and cognitive disorders, decreased functioning and quality of life, mortality, and financial costs to society (Kasckow *et al.*, 2013; Laborde-Lahoz *et al.*, 2015; Lyness *et al.*, 1999).

Previous research suggests that loneliness and depression are associated and often co-occur. Evidence on the association of aging with loneliness and depressive symptoms is contradictory, and there is a lack of longitudinal research in the elder population group. Loneliness may be either a risk factor for depression (Blazer, 2002; Heikkinen and Kauppinen, 2004) or a consequence of mental health problems (Bowling *et al.*, 1989). Some studies suggest a bidirectional association between loneliness and depression (Hsueh *et al.*, 2019; Tiikkainen and Heikkinen, 2005), and others consider depression to be the independent variable, and loneliness as the outcome variable (Dahlberg *et al.*, 2015; Emerson and Jayawardhana, 2016). We decided to select original research that measured

the impact of loneliness on depression in the elderly. Most of the evidence concerning the association between depression and loneliness is based on cross-sectional design studies. Little is known about the temporal association between loneliness and depression (Courtin and Knapp, 2017). To fill the research gaps and to strengthen our knowledge on the impact of loneliness on depression over time, we included only longitudinal studies in this systematic review. We hypothesized that loneliness has an important impact on the new onset of an episode of depressive symptoms and the course of depression.

Methods

This research was conducted following the Preferred Reported Items for Systematic reviews and Meta-Analysis (PRISMA-P) guidelines (Moher *et al.*, 2015). For the purpose of this review, we chose to focus on longitudinal studies in order to investigate the relationship between loneliness (i.e. perceived social isolation or subjective loneliness) and depression in the elderly, more specifically the impact of loneliness on depression in healthy community-dwelling elders over 60 years of age. The search was carried out in July 2020. Several steps were taken in order to select the studies and extract the information (see Figure 1). The databases included were Scopus, PsycInfo, and PubMed. No restrictions on the date of publication or location of the studies were imposed. The keywords and their combination were defined prior to the search. We used a combination of search terms related to our population group of interest, social isolation and loneliness, and depression as a mental health outcome. Predefined keywords included "loneliness AND depress* AND elderly," "loneliness AND depress* AND older," "loneliness AND depress* AND aged," "social isolation AND depress* AND elderly," "social isolation AND depress* AND older," and "social isolation AND depress* AND aged." We searched for the keywords: in title, abstract and keywords in Scopus; in title and abstract in PubMed and abstract in PsycInfo. The combined search yielded 11,081 references. Duplicate records were identified through the electronic search and were removed using the reference manager software package Zotero.

Study eligibility criteria

After duplicates were removed, all titles and abstracts of the remaining studies were screened to select potentially relevant articles. Initially, we included original research in peer-reviewed articles,

written in English, French, Dutch, German, and Italian that provided quantitative data on loneliness and depression. We excluded books, comments, conference papers, editorials, letters, and theses. To meet inclusion criteria, studies had to investigate both loneliness and depression in healthy community-dwelling elders over 60 years of age. Because we were interested in the impact of loneliness on depression, we excluded all articles that considered cognitive impairment as a mental health outcome. We excluded all intervention programs on loneliness and depression.

Subsequently, we decided to select only studies with a focused longitudinal design. Previously, we had excluded "longitudinal" as a search term to avoid the possibility of omitting any articles that, while being longitudinal in design, did not mention the term in the title or abstract.

For the final selection, we had three independent researchers review the full texts of all potentially eligible publications, to be coded as either included or excluded. We included all longitudinal designs that yielded a statistical estimate of the effect of loneliness on depression. Specifically, loneliness has to be measured at baseline and depression at follow-up. We contacted the authors to receive some missing data. In the end, 10 articles were included in this systematic review.

Coding strategy

Two coders independently distinguished the categories for the research design found in the articles. We used two categories to classify the relevant variables: 1) the longitudinal association between loneliness and depressive symptoms (Outcome 1) and 2) the clinical course of depressive symptoms (Outcome 2). The first category included all the results which relate the first measure of loneliness at the beginning of the research and the measure of depressive symptoms at the follow-up to the study. The second category contains all the results that related the clinical course of depressive symptoms (e.g. new onset, remission, and maintenance) during the study, and the measure of loneliness at the beginning of the research. The summary of main findings, the measures used by the studies, and the design of the analyses are reported in Table 1. The association was analyzed using the odds ratios (ORs), bivariate correlation, and β scores. The magnitude of the OR in the present review is discussed on the base of the classification proposed by Chen and colleagues in 2010, which reported as small an OR < 1.5, as medium an OR between 1.5 and 4.9, and as large an OR $\geq$ 5.0.
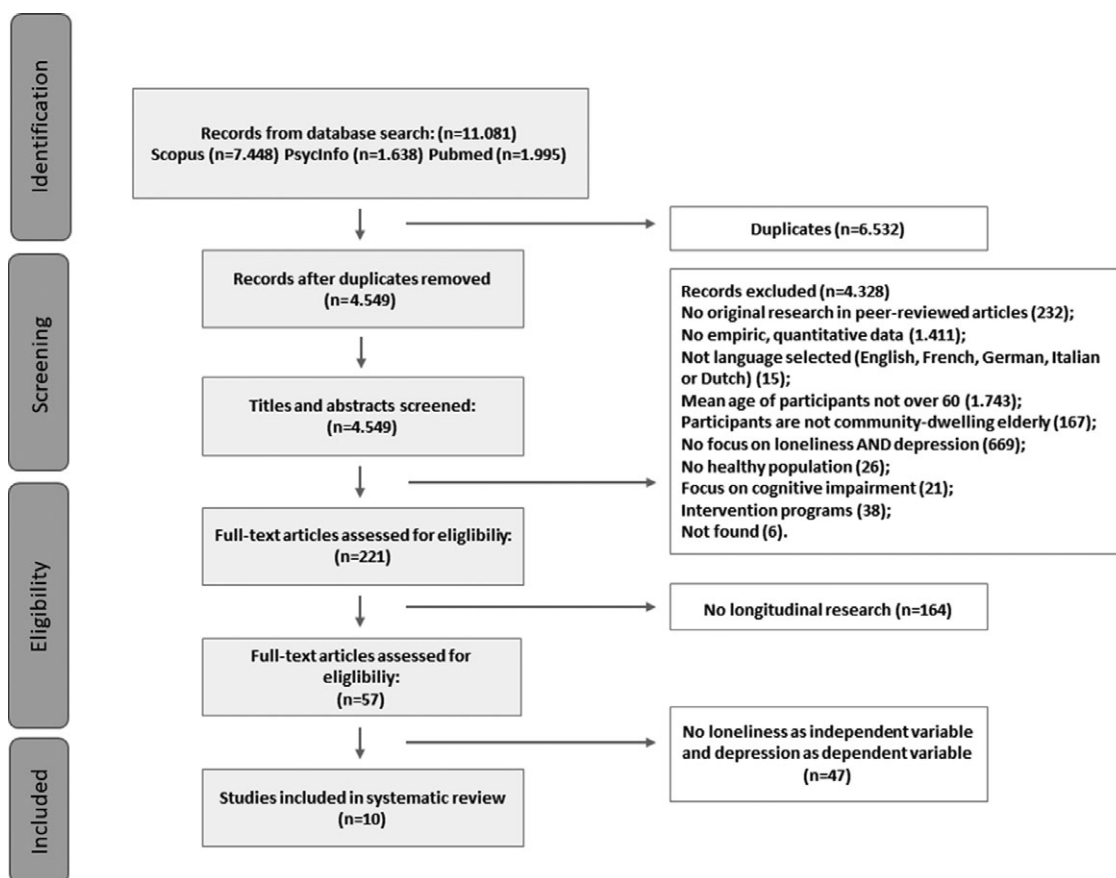
Fig 1. PRISMA flow diagram showing the process used in the review.

Results

The articles included in the review were published between 1992 and 2019, six of which in the last 5 years. Six studies have been conducted in European countries, one study in the UK, one study in the USA, one in Taiwan, and one in Singapore (see Table 2). The overall sample was of over 1000 participants in 7 of the studies. One study relied on a subsample of a harmonized dataset using the results of six longitudinal studies (de la Torre-Luque *et al.*, 2019). The mean age of participants at the end of the research period was ≥ 75 in four studies and ≤ 75 in six studies. Five studies investigated the longitudinal association between loneliness and depressive symptoms (Outcome 1), while two studies concentrated exclusively on the clinical course of depressive symptoms in elderly people (Outcome 2). Three of them reported both clinical course and data on the impact of loneliness on depression over a number of years (Conde-Sala *et al.*, 2019; de la Torre-Luque *et al.*, 2019; Holvast *et al.*, 2015). The studies have taken into consideration covariates such as marital status (Conde-Sala *et al.*, 2019; de la Torre-Luque *et al.*, 2019; Green *et al.*, 1992; Holvast *et al.*, 2015; Segel-Karpas *et al.*, 2018), social network (Green *et al.*, 1992; Holvast *et al.*, 2015; Jeuring *et al.*, 2018; Lim and Kua, 2011; Segel-Karpas *et al.*, 2018; Sjöberg *et al.*, 2013; Steunenberg *et al.*, 2010), activities of daily living (Conde-Sala *et al.*, 2019; de la Torre-Luque *et al.*, 2019; Lim and Kua, 2011; Segel-Karpas *et al.*, 2018); chronic physical diseases (Conde-Sala *et al.*, 2019; Holvast *et al.*, 2015; Hsueh *et al.*, 2019; Jeuring *et al.*, 2018; Steunenberg *et al.*, 2010), quality of life (Green *et al.*, 1992, Hsueh *et al.*, 2019, Lim and Kua, 2011), and age of retirement (Segel-Karpas *et al.*, 2018). Four studies had a follow-up period of 2 years, all of them used the pre- and post-test. Three studies had a follow-up period of 3, 5, and 6 years, all three used the pre- and post-test. Another study had a follow-up length of 6 years (three waves, every 3 years), and the longest longitudinal study had a follow-up period of 14 years (five waves, every 3–4 years). The study that relied on a subsample of a harmonized dataset used the results of six longitudinal studies. The overall follow-up period dated from 1995 to 2013. One study had a

Table 1. Analyzed variables and main findings of the included studies

ARTICLE NUMBER	LONELINESS MEASURE	DEPRESSION MEASURE	TYPE OF ANALYSIS	ANALYSIS SPECIFICATION	STATISTIC	STATISTIC VALUE
1	RTLS	IDS-SR	Multinomial logistic regression	Partial remission versus full remission	OR (95% CI)	OR = 1.20* (1.08–1.34)
			Multinomial logistic regression	Recurrent or chronic versus full remission	OR (95% CI)	OR = 1.26* (1.11–1.42)
			Multinomial logistic regression	Recurrent or chronic versus partial remission	OR (95% CI)	OR = 1.05* (0.94–1.16)
2	Short Loneliness Scale (Hughes *et al.*, 2004)	EURO-D	Multivariate logistic regression	Wave 5 to Wave 6: incidence versus no depression	OR (99% CI)	OR = 1.63** (1.62–1.64)
			Multivariate logistic regression	Wave 5 to Wave 6: persistence versus no depression	OR (99% CI)	OR = 3.10** (3.09–3.11)
			Multivariate logistic regression	Wave 5 to Wave 6: remission versus persistence	OR (99% CI)	OR = 1.39* (1.38–1.39)
3	Revised UCLA Loneliness Scale	Center for Epidemiologic Studies Depression Scale (CES-D)	Stepwise linear regression analysis	Effects of loneliness at T1 on depression at T2	β; p value	$\beta = 0.38$; $p < .001$
			Stepwise linear regression analysis	Interaction between loneliness and depressive symptoms at T1 on depression at T2	β; p value	$\beta = .18$, $p < .001$
4	RTLS	CIDI/IDS-SR	Linear regression analysis	Between baseline loneliness and depression severity at follow-up	β; (CI 95%); p value	$\beta = 0.73$; (0.29–1.16); $p < 0.001$
			Linear regression analysis	Between baseline loneliness and depression severity at follow-up – adjusted for social network size	β; (CI 95%); p value	$\beta = 0.76$ (0.30–1.22); $P < 0.001$
			Linear regression analysis	Between baseline loneliness and depression severity at follow-up – adjusted for social network size, age, gender, marital status, education, neuroticism, cognitive functioning, pain intensity, and disability	β; (CI 95%); p value	$\beta = 0.61$; (0.12–1.11); $p < 0.02$
			Logistic regression analysis	Moderately lonely versus not lonely	OR; (CI); p value	OR = 0.41*; (0.18–0.94); $p = 0.03$

Table 1. Continued

ARTICLE NUMBER	LONELINESS MEASURE	DEPRESSION MEASURE	TYPE OF ANALYSIS	ANALYSIS SPECIFICATION	STATISTIC	STATISTIC VALUE
			Logistic regression analysis	Moderately lonely versus not lonely – adjusted for social network size.	OR; (CI); p value	OR = 0.46[*] (0.20–1.06); $p = 0.07$
			Logistic regression analysis	Moderately lonely versus not lonely – adjusted for social network size, age, gender, marital status, education, neuroticism, cognitive functioning, pain intensity, and disability	OR; (CI); p value	OR = 0.50[*]; (0.20–1.26); $p = 0.14$
			Logistic regression analysis	Severely lonely versus not lonely	OR; (CI); p value	OR = 0.48[*]; (0.20–1.16); $p = 0.10$
			Logistic regression analysis	Severely lonely versus not lonely – adjusted for social network size.	OR; (CI); p value	OR = 0.56[*]; (0.22–1.40); $p = 0.22$
			Logistic regression analysis	Severely lonely versus not lonely – adjusted for social network size, age, gender, marital status, education, neuroticism, cognitive functioning, pain intensity, and disability	OR; (CI); p value	OR = 0.68[*]; (0.25–1.87); $p = 0.46$
			Logistic regression analysis	Very severe lonely versus not lonely	OR; (CI); p value	OR = 0.96[*] (0.93–0.98); $p < 0.001$
			Logistic regression analysis	Very severe lonely versus not lonely – adjusted for social network size, age, gender, marital status, education, neuroticism, cognitive functioning, pain intensity, and disability	OR; (CI); p value	OR = 0.98[*]; (0.94–1.01); $p = 0.22$
5	RTLS	CES-D	Logistic regression analysis	Recurrence of depression in older adults compared to continuous recovery	OR; (CI 95%); p value	OR= 1.1[*]; (1.0–1.3)
6	Feelings of loneliness: "Do you feel lonely?" (0 = disagrees, 1 = agrees, 2 = strongly agrees)	GMS	Chi-squared	Log-linear modeling	OR	OR =1.82[**]

Table 1. Continued

ARTICLE NUMBER	LONELINESS MEASURE	DEPRESSION MEASURE	TYPE OF ANALYSIS	ANALYSIS SPECIFICATION	STATISTIC	STATISTIC VALUE
7	Defined as often or sometimes versus seldom or neve	CPRS	Multivariate logistic regressions adjusted for sex and marital status	Loneliness as risk factor to be depressed at follow-up at 75 (cohort 1901–02)	OR; (CI 95%); p value	OR = 3.81** (1.10–13.20); $p < 0.05$
				Loneliness as risk factor to be depressed at follow-up at 75 (cohort 1930)	OR; (CI 95%); p value	OR = 2.80** (1.23–6.39); $p < 0.05$
8	Multiple measures	CES-D/Euro-D	OR	Transition from no depression symptoms to depression	OR; (CI 95%); Z; p value	OR = 17.76***; (15.966–19.768); $z = 52.80$; $p < 0.001$
				Persistence of depressive episodes	OR; (CI 95%); Z; p value	OR = 5.929***; (5.541–6.344); $z = 51.50$; $p < 0.001$
				Transition from depression to no depression state	OR; (CI 95%); Z; p value	OR = 2.190**; (2.050–2.339); 23.30; $p < 0.001$
9	"Have you felt loneliness during the last week" – 4-point response scale ranged from "no" to "often or always."	Seven items, originated from the CES-D	Correlation	Correlation between loneliness at T1 and depression at T5	r; p value	r = 0.16; $p < 0.001$
10	"Do you feel that at the present moment you are not at all lonely (= 1), fairly lonely (= 2), and very lonely (= 3)?"	GDS	Logistic regression	Lonely versus not lonely on depression at follow-up	OR; p value	OR= 1.39*; $p = 0.003$

Effect size for OR: small* < 1.5; medium** 1.5–4.9; large*** ≥ 5.0.

Table 2. Characteristics of the included studies

ARTICLE NUMBER	TITLE	AUTHORS	YEAR	COUNTRY	SAMPLE SIZE	RANGE	FOLLOW-UP AT	NUMBER OF MEASURES	TIME SPAN BETWEEN MEASURES
1	A 6-year prospective study of the prognosis and predictors in patients with late-life depression	Jeuring *et al.*	2018	The Netherlands	201	≥ 60	6 years	2	6 years
2	Course of depressive symptoms and associated factors in people aged 65 + years in Europe: a 2-year follow-up	Conde-Sala, et al	2019	Spain	23.201	≥ 65	2 years	2	2 years
3	Loneliness and depressive symptoms: the moderating role of the transition into retirement	Segel-Karpas, et al	2018	USA	2.329	30–96	2 years	2	2 years
4	Loneliness is associated with poor prognosis in late-life depression: longitudinal analysis of the Netherlands study of depression in older persons	Holvast *et al.*	2015	The Netherlands	285	64.5–76	2 years	2	2 years
5	Personality predicts recurrence of late-life depression	Steunenberg *et al.*	2010	The Netherlands	91	≥ 55	6 years	3	3 years
6	Risk factors for depression in elderly people: a prospective study	Green *et al.*	1992	UK	1.070	≥ 85	3 years	2	3 years
7	Secular changes in the relation between social factors and depression: a study of two birth cohorts of Swedish septuagenarians followed for 5 years	Sjöberg *et al.*	2013	Sweden	392 (in 1976) 499 (in 2005)	≥70	5 years	2	5 years
8	Stability of clinically relevant depression symptoms in old-age across 11 cohorts: a multi-state study	de la Torre-Luque, de la Fuente, Sanchez-Niubo *et al.*, 2019	2019	Spain	41.362	≥65	Multiple values	Multiple values	Multiple values
9	A longitudinal, cross-lagged panel analysis of loneliness and depression among community-based older adults	Hsueh *et al.*	2019	Taiwan	3.920	60–96	14 years	5	3–4 years
10	Living alone, loneliness, and psychological well-being of older persons in Singapore	Lim and Kua	2011	Singapore	2.799	≥ 55	2 years	2	2 years

follow-up length of 4 years (three waves), another 6 years (four waves), another one 9 years (four waves), and three studies had a length of 11 years (3, 6, and 6 waves).

All studies used validated scales, such as the Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977), the Geriatric Mental Scale (GMS) (Copeland *et al.*, 1976), the Comprehensive Psychopathological Rating Scale (CPRS) (Arfwidsson *et al.*, 1971; Åsberg *et al.*, 1978), the Inventory of Depressive Symptoms Self-Report (IDS) (Rush *et al.*, 1996), the Composite International Diagnostic Interview (CIDI) (Wittchen *et al.*, 1991), the Geriatric Depression Scale (GDS) (Sheikh and Yesavage, 1986), and the EURO-D (Guerra *et al.*, 2015) to measure depressive symptoms. Loneliness was measured using both validated scales present in literature and tailored items. Validated scales utilized included the UCLA Loneliness Scale (University of California, Los Angeles) (Russell *et al.*, 1980), the Rasch-Type Loneliness Scale (RTLS) (De Jong-Gierveld and Kamphuls, 1985), and the Short Loneliness Scale of Hughes and colleagues (Hughes *et al.*, 2004), while five others utilized a single question tailored item regarding the subjective feeling of loneliness (e.g. Do you feel lonely?). Seven studies report on the association between loneliness and depression using the OR, one uses the β scores, another utilized Pearson's correlation, and yet another study reported both OR and β scores.

As a result, we separated the main findings of the studies into Outcome 1 and 2 (see Table 1 for main findings).

Outcome 1 – the longitudinal association between loneliness and depressive symptoms

In this category, we included eight studies that investigated the temporal association between loneliness and depressive symptoms. All articles included in this category confirmed a positive and significant association between loneliness at baseline and depression at follow-up. Five studies reported the OR in their analysis. Two articles found a small but significant association ($r = 0.16$, $p < 0.001$; $OR = 1.39$, $p = 0.003$) (Hsueh *et al.*, 2019; Lim and Kua, 2011). Three articles found a medium effect size ($OR = 1.63$; $OR = 1.82$; $OR = 3.81$, $p < 0.05$) (Conde-Sala *et al.*, 2019; Green *et al.*, 1992; Sjöberg *et al.*, 2013) and one article found a large effect size ($OR = 17.76$, $p < 0.001$) (de la Torre-Luque *et al.*, 2019). Two studies that used the β score suggest that loneliness is a significant determinant of depressive symptoms ($β = 0.38$, $p < .001$; $β = 0.73$, $p < 0.001$) (Holvast *et al.*, 2015; Segel-Karpas *et al.*, 2018).

Outcome 2 – the clinical course of depressive symptoms

An unfavorable course of depression was associated with loneliness at baseline. In one study (Holvast *et al.*, 2015), the findings suggested that acute levels of loneliness result in a slimmer chance of achieving remission from a depressive state. The effect size between very severe levels of loneliness and depressive symptoms is higher ($OR = 0.96$, $p < 0.001$) compared to severe ($OR = 0.56$, $p = 0.22$) and moderate ($OR = 0.41$, $p = 0.03$) loneliness levels.

At follow-up, two studies (Jeuring *et al.*, 2018; Steunenberg *et al.*, 2010) analyzed the absence or presence of a depression diagnosis in the elderly subjects who had been diagnosed with depression at baseline. Although the effect size was small, both studies found that loneliness was a significant predictor of recurrence of depression ($OR = 1.26$; $OR = 1.1$) at the end of the observation period.

Similarly, one study analyzed the effect of, from not feeling lonely at baseline, to remission of depression at follow-up (Conde-Sala *et al.*, 2019). Findings suggested a small association ($OR = 1.39$) between not feeling lonely and the recurrence of depression. Namely, those who felt less lonely had a higher probability of not feeling depressed at follow-up, compared to those who experienced a persistent condition of depression at the end of the study.

Two studies focused on the association between loneliness at baseline and persistence of depression at follow-up, by comparing depressed and non-depressed patients (Conde-Sala *et al.*, 2019; de la Torre-Luque *et al.*, 2019). Research findings show that those who were still depressed at follow-up differed from those who had never been depressed, as they had experienced higher levels of loneliness. Both articles reported a medium effect size ($OR = 3.10$; $OR = 5.929$).

Discussion

This study aimed to offer a literature review about the longitudinal effect of loneliness on depressive symptoms in older adults. In agreement with previous literature, we conclude that loneliness was by far a strong stressor on depressive symptoms. All analyses revealed an association between loneliness and other depressive symptoms, or an even more unfavorable course of depression.

Overall, we can discuss the main findings of the current review from three different perspectives.

Firstly, loneliness appears to represent a risk factor for the development of depressive symptoms

in old age. All the studies included in the review that investigated the temporal association between the two variables (Conde-Sala *et al.*, 2019; de la Torre-Luque *et al.*, 2019; Green *et al.*, 1992; Holvast *et al.*, 2015; Hsueh *et al.*, 2019; Lim and Kua, 2011; Segel-Karpas *et al.*, 2018; Sjöberg *et al.*, 2013) found that loneliness is a predictor of depression, as it facilitates the occurrence of depressive symptoms. Secondly, following the studies' results that focused on the clinical course of depression and its longitudinal association with loneliness (Conde-Sala *et al.*, 2019; de la Torre-Luque *et al.*, 2019; Holvast *et al.*, 2015; Jeuring *et al.*, 2018; Steunenberg *et al.*, 2010), we can affirm that loneliness plays a role in worsening depression. Those who had experienced more loneliness had a higher probability of showing an increase in depressive symptoms. Finally, the longitudinal effect of loneliness also appears to hinder remission from depression in the elderly. In fact, people who reported feeling lonely were more likely to maintain feelings of depression throughout the study.

All studies clarify the temporal order of loneliness and depression. However, causality association between loneliness and depression has to be investigated further. Indeed, an up-to-date bidirectional relationship has been found in several studies (Hsueh *et al.*, 2019; Tiikkainen and Heikkinen, 2005). This systematic review identifies loneliness as an important factor that has an impact on depressive symptoms in old age. Nevertheless, among the results of the included studies, we can observe a heterogeneity regarding the effect size outcome. This heterogeneity could be due to covariates included in the analysis of the research. Indeed, almost all the studies have implemented multivariate analyses in their research design. The observed heterogeneity in effect size may have been caused by various covariates analyzed and their impact on depressive symptoms.

Age-related conditions, such as cognitive impairment, impaired physical mobility, impairment in activities of daily living (ADL), financial difficulties, bereavement, living conditions, and personality traits such as lack of mastery and neuroticism, can cause difficulties in the maintenance of relationships and may act as potential covariates that moderate the association between loneliness and depression. Previous studies indicated age and female gender as important variables, but because of the small sample of articles retrieved, we could not further investigate age and gender differences. Although living alone and loneliness are well-distinguished concepts, a higher number of depressive symptoms have been found in those living alone rather than in those living with others (Lim and Kua, 2011). Living in a collectivist or individualist culture can certainly

moderate the effect of loneliness on depression, but the final sample of this systematic review is too small to suggest any conclusions. One study highlights the importance of cultural and socioeconomic aspects (Conde-Sala *et al.*, 2019). According to this study, different welfare programs can play a significant role. They indicate the need for countries, especially in Eastern and Southern Europe, to provide greater support, resources, and social benefits to the elderly (Conde-Sala *et al.*, 2019). As one study (Segel-Karpas *et al.*, 2018) demonstrated, employment provides social engagement and social support and acts as a protective factor that moderates the negative effect of loneliness on depressive symptoms. Future research should aim to provide interventions that enhance social engagement in the lives of the elderly. Lifestyle, daily routine, and social environment change a lot during the transition into retirement and could have a negative effect on both loneliness and depression.

From the present literature review, there is a lack of research results regarding moderators that can influence the association of loneliness and depressive symptoms, both in negative and positive ways. There is an urgent need to study all factors that could decrease the detrimental influence of loneliness on depression in the elderly.

Moreover, some limits that have been found in the included studies may have been caused by the mortality rate of the sample and the measures used to detect loneliness. In longitudinal studies with the elderly, numerous studies have to face a high rate of missing participants in following waves due to cognitive impairment and mortality. One study had attrition that was almost twice as high in the depressed group than in the non-depressed group: nearly 47% of the depressed elderly were lost due to mortality (Jeuring *et al.*, 2018). This result confirms previous results that depression is an important risk factor for mortality. This high loss of participants by the end of the study could have affected the association between the variables in the studies. Some studies measured loneliness via a single item (de la Torre-Luque *et al.*, 2019; Hsueh *et al.*, 2019; Sjöberg *et al.*, 2013) which probably is not sensitive enough to consider the loneliness in elders and may have led to underreporting of loneliness. The research included in our review focuses on community-dwelling elderly people. This possible source of bias raises questions about extremely lonely people who may have been less motivated to participate or more difficult to recruit.

Loneliness does increase with age, not because of age, but because of the increasing of mental and physical disability and the decreasing of social integration (Jylhä, 2004). Not much is known about the relationship between loneliness and depression, and

even less research has been found on variables that could moderate this association. Most of the articles included in the present review consider only subjective feelings of loneliness, measured by validated scales or tailored items, omitting more objective measures. Objective and subjective loneliness are related, although this association is relatively modest (Hughes *et al.*, 2004). Future studies could investigate the relation between depression and both subjective loneliness and social isolation, or how loneliness moderates the relationship between social isolation and depression. Loneliness is not an irreversible aspect of getting old, so evidence-based interventions should be developed to prevent and treat the detrimental impact of loneliness on depression, development of dementia, and risk of mortality in the elderly. Nowadays, older adults have more access to a larger external social reserve, due to technological developments (Sjöberg *et al.*, 2013). Technological solutions and low-tech interventions can be used to mitigate feelings of loneliness. The provision of equipment and training to both caregivers and the elderly could improve the disparity in access to, and knowledge of, digital resources. Implementation of interventions using new technological means could tackle the devastating effects of loneliness, promote participation and social network enrichment, enhance life satisfaction, and improve the overall well-being and quality of life of lonely elders.

As proven by literature, loneliness has detrimental effects on both physical and mental health, and COVID-19 measures may even have increased the dangerous consequences in this already vulnerable group of elders (Webb, 2020). As a consequence, the need to develop and implement evidence-based interventions is more urgent than ever.

Conflict of interest

None.

Description of authors' roles

B.A.L. Van As performed the research of the articles, reviewed titles and abstracts, analyzed and interpretated the results, and wrote the paper. E. Imbimbo analyzed and interpreted the results and wrote the paper. A. Franceschi performed the research of the articles and reviewed titles and abstracts. E. Menesini did the critical revision of the article and gave final approval of the article. A. Nocentini envisaged the problem, coordinated the research, did the critical revision of the article, and gave final approval of the article. All the authors revised the manuscript.

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